

From teens to old age: psychiatry strives to help



Treatment challenges across the life course was the theme for the 10th Latest Advances in Psychiatry Symposium, held in London in March. Speakers addressed issues facing psychiatrists caring for patients from the teenage years right through to old age. Steve Titmarsh provides an overview of the key issues raised during the meeting.

The annual Latest Advances in Psychiatry Symposium began in 2002: it was the idea of the late Professor Robert Kerwin who was instrumental in putting the programme together each year, on behalf of the Royal College of Psychiatrists' Psychopharmacology Special Interest Group (PSIG) in collaboration with *Progress in Neurology and Psychiatry*. Each year delegates have been treated to lectures from some of psychiatry and psychopharmacology's finest minds, in particular from the keynote speakers who have included: Professor Jules Angst; Nobel Laureate, Professor Arvid Carlsson; Professor Tim Crow; Professor Sir David Goldberg; Professor Leslie Iversen; Professor Malcolm Lader; Professor Sir Robin Murray; Professor Gerald Russell; and Professor Sir Michael Rutter.

The 10th Symposium followed that tradition on the theme of 'Treatment challenges across the life course'. Keynote speaker, Professor Ian Goodyer, from the University of Cambridge, challenged the ability of the current diagnostic systems to provide sufficient insight into the causes of psychiatric illness and proposed a more subjective and scientific approach, which might provide greater clarity about the nature of psychiatric disorders and help improve treatment success rates from the somewhat disappointing levels generally achieved at the

moment. (A report of Professor Goodyer's lecture was published in the July/August 2011 issue of *Progress in Neurology and Psychiatry*.)

Professor Philip Asherson, from the Institute of Psychiatry in London, discussed the changing face of attention deficit-hyperactivity disorder (ADHD) as sufferers transitioned from childhood to adolescence, and countered the idea that the condition was hard to diagnose.

Dr Ian Jones, from Cardiff University, reviewed the treatment of psychiatric disorders in women in the perinatal period. He emphasised the importance of not sitting on the fence when it came to advising women about medication during a crucial time in their lives and the lives of their children, despite the relative lack of clinical data to support some aspects of the pharmacological management of these patients.

Professor Clive Holmes, from the University of Southampton, catalogued the numerous and varied efforts of researchers to devise a means of combating dementia. He concluded that prevention, if feasible, may hold the greatest promise for a means to manage a problem that will face greater numbers of people as the population continues to age.

Finally, Dr Michael Craig, from the Institute of Psychiatry in London, described some emerging data that hold out the possibil-

ity that oestrogen may provide some help for women with mood disorders around the time of the menopause.

All-in-all, the day provided a comprehensive look at the challenges psychiatrists face in their day-to-day practice caring for people with mental illness, from teenagers with so much potential both physically and mentally, through to the latter years of life when many may feel people are mentally, as well as physically, on a downward spiral. This short report covers some of the key aspects of each lecture.

ADHD from adolescence to adulthood

ADHD is a common behavioural disorder that is associated with significant adult psychopathology, social and academic impairments and the risk of negative long-term outcomes, Philip Asherson, Professor of Molecular Psychiatry at the MRC Social, Genetic and Developmental Psychiatry Research Centre and Honorary Consultant Psychiatrist at the Institute of Psychiatry in London, told delegates.

Prevalence among children in the UK is around 3-5 per cent and around 1 per cent of children are diagnosed and treated in the UK. Symptoms persist into adult life and can cause significant clinical impairments. But the condition is often mistaken for other trait-like condi-

tions, particularly personality disorders and bipolar disorder. Indeed, definitions of bipolar disorder can be wide enough to overlap with those of ADHD, Professor Asherson said. However, ADHD is no more difficult to diagnose in adults than other common mental health disorders, he argued, and can be successfully treated in most cases.^{1,2}

Typically, young adults with ADHD complain of a mind so active they have difficulty going to sleep because they are distracted by the cacophony going on in their head. They may also be woken up sometimes with a constant feeling that something needs to be done. For this reason, they also find it difficult to sit still for any length of time and have problems with queues, to the extent that they may walk miles rather than wait in a queue for a bus, for example.

Screening instruments tend to overdiagnose ADHD, so a good clinical interview is needed: proper assessment probably takes about two hours, Professor Asherson said. It is useful to look at IQ and reading ability. While it is a good idea to ask patients if they have problems like not being able to sit still for a length of time, they should also be asked why they feel like that: the behavioural items are not the diagnosis itself. As Professor Asherson explained, ‘you want to get to the phenomenological causes behind the symptoms’.

Symptoms are not episodic, they are constant and pervasive. So even though a patient may function better in some environments than others, the symptoms are always with them. People with ADHD almost always have low self-esteem, probably related to the fact that it is a lifelong condition with many negative experiences contributing to these feelings. Performance variation/variability is common, so people with the

Stop medication

– abrupt discontinuation may lead to withdrawal phenomena or withdrawal precipitation of episode

Switching

– involves exposure to two medications and may not be efficacious

Continuation

– close monitoring of foetus/neonate needed

Table 1. Conception while on medication – options to consider

condition are often good at some things that have meaning or are salient but do not perform well at others, particularly those with relatively low reward content. There is a wide range of disorders that can co-occur and develop alongside ADHD.

Sometimes people may realise only in later life that they could be suffering with symptoms of ADHD, perhaps when a younger relative has been diagnosed. Some people are quite seriously impaired and it can explain all sorts of strange behaviours while others may be only mildly impaired and much thought may be needed on whether to treat them or not. About 80 per cent of adults with ADHD describe a significant level of mood instability.

References

1. Kooij SJJ, Bejerot S, Blackwell A, *et al.* European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. *BMC Psychiatry* 2010;10:67.
2. Nutt DJ, Fone K, Asherson P, *et al.* Evidence-based guidelines for management of attention-deficit/hyperactivity disorder in adolescents in transition to adult services and in adults: recommendations from the British Association for Psychopharmacology. *J Psychopharmacol* 2007;21:10-41.

Prescribing in pregnancy

Pregnancy can have a dramatic effect on existing mental illness, and childbirth is a potent trigger for mental illness, Dr Ian Jones, Reader in Perinatal Psychiatry and Honorary Consultant Psychiatrist at the MRC Centre for Neuropsychiatric Genetics and Genomics

at Cardiff University, told delegates. Furthermore, it does not seem to be related particularly to whether women stop or change medication.

During pregnancy a number of factors may affect drug pharmacokinetics and pharmacodynamics. For example, absorption may change, particularly among those who have vomiting problems. Increased volume of distribution may have an impact. Also metabolism and clearance of drugs may be different during pregnancy.

As with other areas of psychiatry, clinical decision making is hampered to an extent by the lack of an evidence base, in part as a result of restrictions on clinical studies, such as pregnant and breast-feeding women being specifically excluded from drug trials. However, Dr Jones pointed out that from the limited data that do exist, there does not seem to be strong evidence that psychiatric disorders respond differently to drug treatment during the perinatal period than they do at other times in women’s lives.

It is important to remember that up to 80 per cent of women are exposed to medications during pregnancy; the malformation rate among mentally ill women treated with drugs is 2-4 per cent and 50 per cent of pregnancies are unplanned. Dr Jones advised that all women should be treated with the possibility of pregnancy in mind during their reproductive years and contraception should be

discussed with every woman treated.

With medication, the focus tends to be on teratogenicity but, explained Dr Jones, there are other risks including risk of neonatal toxicity and withdrawal and risk of longer term neurobehavioural/cognitive problems. The illness itself carries risks too. For example: untreated illness may affect birth weight and gestational age at delivery; there may be a detrimental effect of stress in pregnancy on the foetus, and the illness may impact on mother-infant attachment and later infant development.

Equally, stopping medication is not without consequences. For example, *Viguera et al.* showed that the risk of recurrence of mental illness was much higher among women with a history of bipolar disorder when medication was stopped compared with continuing it during pregnancy.¹

Decisions about medication ultimately lie with the woman, but as professionals, women may look to us for guidance and we should not be afraid to say what we think while at the same time being careful to document what we do, Dr Jones advised. Every decision is an individual one, guided by general principles (see Table 1).

Reference

1. Viguera AC, Whitfield T, Baldessarini RJ, et al. Risk of recurrence in women with bipolar disorder during pregnancy: prospective study of mood stabilizer discontinuation. *Am J Psychiatry* 2007;164:1817-24.

Search for Alzheimer's disease treatment continues

Many avenues have been explored in the search for a treatment, or even better a potential cure, for Alzheimer's disease. Sadly, so far none has borne real fruit or at least provided a solution that is free from side-effects that preclude widespread use, Clive Holmes,

Professor of Biological Psychiatry at the University of Southampton, told delegates.

Research into future treatments for Alzheimer's disease has focused mainly on trying to stop development of, or to break up, amyloid plaques. Amyloid is a small molecule, part of larger amyloid precursor protein (APP), which accumulates to form plaques in the brain, which are thought to result in neuronal cell death, leading to cognitive decline. Alpha secretase cleaves APP in half leaving one molecule that is thought to protect against Alzheimer's disease; as we age, other enzymes – beta secretase and gamma secretase – cleave APP at other points, which is postulated to lead to accumulation of amyloid in the brain. So some research has pursued the idea of inhibiting beta or gamma secretase or encouraging alpha secretase as a means of stopping the build up of amyloid plaques.

Another major anti-amyloid approach has been the development of immunisation techniques that have been shown to remove the build up of amyloid plaques in the brains of patients with Alzheimer's disease. However, clinically the results have been at best equivocal, and often side-effects have emerged that preclude the widespread use of the compounds developed.

As the search for an effective, well-tolerated treatment has so far proved unsuccessful, Professor Holmes felt prevention may offer better prospects – helping people before they have the disease or very early on. That seems to be the way the diagnostic systems are moving as well. For example, the proposed DSM-5 includes major neurocognitive disorder (Alzheimer's disease subtype) and minor neurocognitive disorder (Alzheimer's disease subtype; mild cognitive impairment).

The Alzheimer's Association goes further, describing preclinical Alzheimer's disease – without even subjective memory impairment – diagnosed on the basis of raised amyloid or tau levels in lumbar spine samples. So this would include people who pre-clinically do not even have the disease, Professor Holmes explained.

Inflammation has been implicated in the aetiology of Alzheimer's disease and so TNF alpha inhibition has been explored, with some suggestion of success, but more work is needed before a treatment emerges. Other lines of research have included nerve repair, and vascular aspects using compounds such as folic acid, angiotensin converting enzyme (ACE) inhibitors and drugs to alter cholesterol metabolism. Work has also been done on reducing mitochondrial damage. But as yet there is insufficient evidence to support the use of these approaches in a clinical setting.

For now, the best general advice seems to be to take regular mild exercise – studies from Australia show that regular physical activity, *eg* just a 20-minute walk four to five times per week that is not strenuous enough to cause stress, is a protective factor: 'so a simple message to patients with mild cognitive impairment is to tell them to stop having the newspaper delivered and go and get it themselves,' Professor Holmes suggested.

Reference

1. Chou RC. Presented at American College of Rheumatology 2010 Annual Scientific Meeting, Atlanta, Nov 6-11, 2010.

Potential roles for oestrogen in dementia and depression?

Although studies carried out so far are relatively small, evidence seems to be emerging that oestrogen

therapy may impact on the development of dementia and be beneficial for some women with mood disorders in the perimenopausal period. However, Dr Michael Craig, Senior Lecturer at the Institute of Psychiatry and Honorary Consultant Psychiatrist at the Maudsley Hospital in London, told delegates that timing of treatment appears to be a key factor.

The relationship between hormone replacement therapy (HRT) and the development of dementia, and Alzheimer's disease in particular, is by no means clear, partly because of a multitude of factors at play in the aetiology of the disease. However, the so-called critical

period hypothesis suggests that oestrogen therapy may be beneficial if initiated early, around the time of the menopausal transition. But there is currently no evidence that oestrogen can treat the symptoms of Alzheimer's disease.

Mechanisms by which HRT might exert its effects in dementia have yet to be elucidated. However, work by Dr Craig's group points to possible effects on central cholinergic function, which may have effects on memory.¹

Limited research suggests there may be a subgroup of women vulnerable to developing mood and other psychiatric disorders at times of hormonal change, who may benefit from oestrogen

therapy for depression. Similarly, women with depression during the perimenopausal period may benefit from oestrogen therapy. But the evidence does not suggest a benefit during the postmenopausal period, and does not currently support the use of oestrogen as primary therapy for clinical depression. A multidisciplinary, tertiary referral service (the Female Hormone Clinic) has been launched at the Maudsley Hospital to identify and treat this subgroup.

Reference

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